REMARKS

In response to the Final Office Action mailed by the PTO on September 27, 2007, favorable reconsideration is respectfully requested in view of the above amendments and the following remarks. Claims 16 and 17 are pending and currently under examination in the application. Without acquiescence in any rejection, claims 16 and 17 have been amended to more particularly point out and distinctly claim certain embodiments encompassed by Applicant's disclosed subject matter. No new matter has been added by the present amendment. Support for the present amendment may be found in the application as originally filed, for example, at page 2, lines 20-21; at page 3, lines 3-6 and page 3, line 16 through page 4, line 7; at page 5, line 25 through page 6, line 6 and page 6, lines 10-17 and 21-23; at page 14, lines 4-24; at page 22, lines 23-27; and elsewhere, including in the Examples.

REJECTIONS UNDER 35 U.S.C. § 103(A)

Claims 16 and 17 stand rejected under 35 U.S.C. § 103(a) for alleged obviousness over Cole (1999 *Biotechniques* 26:748) in view of Coen *et al.* ("The Polymerase Chain Reaction," in Ausubel *et al.*, (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, Inc., Chapter 15, Sections 1-8, 2003). The PTO asserts that Cole teaches gellan electrophoresis gels having concentrations as low as 0.03% and more typically 0.1%, but concedes that Cole does not teach gellan gels comprising DNA polymerase, dNTPs, and a target nucleic acid. The PTO then asserts that Coen *et al.* teach performing PCR reactions with a mixture of target nucleic acid, DNA polymerases, and dNTPs, and *afterwards* displaying the PCR reaction products on an appropriate gel. The PTO further alleges that a person skilled in the art would have been motivated to combine the Cole gellan electrophoresis gel for *displaying* the PCR products of Coen *et al.*

Applicant traverses this rejection. The present embodiments are directed in pertinent part to a nucleic acid amplification reaction mixture for use in nucleic acid amplification, comprising water, gellan at a concentration above 0.005 wt% based on the weight of water, a DNA polymerase, dNTPs, and a target nucleic acid, wherein the nucleic acid

amplification reaction mixture amplifies the target nucleic acid. In certain further embodiments template-dependent nucleic acid amplification is of enhanced sensitivity.

Applicant submits that the present claims satisfy the requirements for non-obviousness under 35 U.S.C. § 103(a). More specifically, including for reasons given in the application and also previously made of record, the presently claimed subject matter relates to the unexpected discoveries that a polynucleotide amplification reaction can be conducted in the presence of gellan despite teachings in the art that suggest otherwise, and that such template-dependent nucleic acid amplification is of enhanced sensitivity, *i.e.*, lower levels of nucleic acid molecules can be amplified when gellan is present than can be amplified in the absence of gellan (*e.g.*, specification at page 7, lines 2-4).

Applicant therefore submits that the PTO has not established a *prima facie* case of obviousness. (*See In re Mayne*, 104 F.3d 1339, 1341-43 (Fed. Cir. 1997), PTO has the burden of showing a *prima facie* case of obviousness). The PTO must show that all of the claimed elements were known in the prior art, that a person skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and that the combination would have yielded nothing more than predictable results to such a skilled person. *KSR International Co. v. Teleflex Inc.*, 550 U.S. __,__, 82 USPQ2d 1385, 1395 (2007), No. 04-1350 4, 14, (U.S. April 30, 2007). Additionally, the PTO must show that the person skilled in the art would have had a reasonable expectation of success in arriving at the claimed subject matter. M.P.E.P. § 2143.02 (citing *In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986)).

In the instant case, the PTO fails to provide evidence or reasoning as to why the skilled person would reasonably have expected *successfully* to combine the recited elements. "A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art." *KSR v. Teleflex*. Specifically, prior to the instant application, it was understood in the art that the presence of gellan was incompatible with a nucleic acid amplification reaction (see, *e.g.*, specification at page 5, line 25 through page 6, line 6) and the PTO fails to point to any knowledge in the art that even remotely suggests that such a reaction might proceed with gellan present. In its allegation that the presently claimed

subject would have been obvious to the skilled person, the PTO impermissibly relies on hindsight in view of the instant application.

As noted above, the instant embodiments relate to a nucleic acid amplification reaction mixture, where as disclosed in the specification and recited in the claims, "amplification" refers to the making of one or more copies of a target nucleic acid or a fragment thereof, and a nucleic acid "amplification reaction" is a template-dependent *in vitro* enzyme-catalyzed reaction for increasing the number of target polynucleotides (*see, e.g.,* page 6, lines 6-14 of the specification). As commonly known in the art, a reaction may be characterized, by way of example, as a change in the arrangement of atoms or molecules to yield substances of different composition and properties.

According to the understanding of a person skilled in the art, the presently amended claims therefore expressly comprise an ongoing nucleic acid amplification reaction (*i.e.,* there is a change taking place in the arrangement of atoms or molecules). By contrast, the PTO asserts nothing more than that a skilled person might have been motivated to use a gellan electrophoresis gel not in such an ongoing reaction, but instead merely to display and analyze the products produced by such a reaction *after* the actual reaction has terminated and therefore ceases to be.

Neither Cole nor Coen *et al.*, alone or in combination, teach or in any way suggest a nucleic acid amplification reaction mixture such as a mixture comprising gellan at concentration above 0.005% wt% based on the weight of water, a PCR mixture (*e.g.*, a DNA polymerase, dNTPs and a target nucleic acid as template), and having the presence therein of an active, ongoing nucleic acid amplification *reaction*. In particular, Cole does not teach a nucleic acid amplification reaction in gellan, but is limited to describing use of a gellan electrophoresis gel merely for displaying nucleic acids. Coen *et al.* do not remedy this deficiency of Cole, because Coen *et al.* fail to describe or even remotely suggest the use of gellan, much less to suggest performing an amplification reaction in the presence of gellan. Applicant wishes to emphasize, as also previously made of record, that the ongoing act of *amplifying* a nucleic acid in a nucleic acid amplification reaction mixture that comprises gellan, as recited in the present claims, is temporally distinct from the mere *display* of pre-formed amplification products that is

alleged by the Action. The PTO therefore fails to establish that the presently recited nucleic acid amplification reaction mixture would have been obvious in view of the state of the art at the time of filing the instant application.

The PTO further fails to show why a person of ordinary skill in the art would have had a reasonable expectation of successfully arriving at the presently claimed reaction mixture merely by combining the cited references, or using any other knowledge in the art. As discussed above and for reasons also previously made of record, the presently claimed subject matter derives from the surprising result that a nucleic acid amplification reaction can proceed in the presence of gellan. As noted by the PTO (Action, at page 4), the specification teaches that gellan sequesters Mg^{2+} (*e.g.,* page 5, line 25 through page 6, line 6) and a person skilled in the relevant art regards Mg^{2+} as a critical ingredient in nucleic acid amplification reactions. Applicant respectfully disagrees, however, with the PTO's assertion that Mg^{2+} is sequestered merely during gellan formation (the Action, page 4). Rather, the specification teaches that intact gellan polymers, or gellan fragments, sequester Mg^{2+} (*e.g.,* page 5, line 26), and Doner (as cited in the specification and of record) teaches that continued Mg^{2+} sequestration is critical for maintaining gellan in its intact form, since gellan polymer is solubilized by incubation with Mg^{2+} chelating agents (*e.g.,* specification at page 5, line 27 through page 6, line 2). From the understanding that gellan polymers or gellan fragments sequester Mg^{2+}, it is submitted that a person of ordinary skill in the art would not have reasonably expected a divalent cation-dependent nucleic acid amplification *reaction* (*e.g.,* PCR) to proceed in the presence of gellan.

The PTO has also failed to show an explicit, apparent reason as to why the skilled person would combine the teachings as allegedly disclosed in the cited references, or any other knowledge in the art, to arrive at the subject matter of the instant claims. There is nothing in either Cole or Coen *et al.* that suggests the surprising results as disclosed in the present specification, and encompassed in the present claims. Instead, Cole if anything teaches away from the claimed subject matter, and therefore provides the skilled person with no apparent reason to combine these references for achieving *amplification* of nucleic acids in the presence of gellan.

In brief summary of the evidence previously detailed on the record, Cole teaches that gellan is not an appropriate electrophoretic medium if it interferes with the intended use of the nucleic acid. Given Cole, the skilled person therefore would not regard gellan as compatible for use in a nucleic acid amplification reaction mixture such as the divalent cation-dependent polynucleotide amplification reaction (*e.g.*, PCR) discussed herein. Cole also teaches that divalent cations, which as noted herein are essential for nucleic acid amplification reactions such as those described in Coen *et al.*, weaken gellan gels, making the gellan gels unsuitable for their intended use. Furthermore, a person of ordinary skill in the art would not be motivated to produce a nucleic acid amplification *reaction* based on the disclosure of Cole, who describes preparation of nucleic acid samples in an electrophoresis sample buffer containing a known chelating agent (*i.e.*, for cations such as Mg^{2+}), EDTA, which would be expected to interfere with the amplification reaction. Coen *et al.* do not remedy the deficiencies of Cole, as Coen *et al.* are utterly silent on the use of gellan. The knowledge in the art regarding the importance of divalent cations such as Mg^{2+} to nucleic acid amplification reactions such as PCR thus provides no apparent reason to use the gellan described in Cole for such amplification, and as discussed here, if anything teaches away from such use.

For the reasons provided herein and previously made of record, Applicant submits that the PTO has failed in each required basis to establish a *prima facie* case of obviousness under 35 U.S.C. § 103. Claims 16 and 17 therefore satisfy the statutory requirements of non-obviousness, and Applicant respectfully requests reconsideration and withdrawal of the rejection of these claims.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All the claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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